

IN THE CLAIMS:

1. (Original) An assemblage comprising a substantially biologically inert proto-drug and a substantially biologically inert activation drug, whereby the proto-drug comprises a differentially selective moiety, a toxic moiety and a cap moiety and whereas the moieties of the proto-drug are linked together in such a manner as to make the proto-drug itself substantially inert.
2. (Original) A process for the preparation of a substantially biologically inert proto-drug whereby the process comprises:
 - (a) selection of a differentially concentrating moiety by a method chosen from the group consisting of differential HPLC, differential chromatography, and in vivo differential rate analysis;
 - (b) selection of a toxic moiety by a method chosen from the group consisting of in vitro testing, in vivo testing and evaluation of published lists of toxic moieties;
 - (c) selection of a cap moiety by a method chosen from the group consisting of in vitro testing, in vivo testing and evaluation of published lists of reagents with the toxic moiety; and
 - (d) linking the differentially concentrating moiety, the toxic moiety, and the cap moiety in such a manner as to make the proto-drug itself substantially biologically inert.
3. (Original) A process for the preparation of an assemblage, whereby the process comprises:

- (a) selection of a differentially concentrating moiety by a method chosen from the group consisting of differential HPLC, differential chromatography, and in vivo differential rate analysis;
 - (b) selection of a toxic moiety by a method chosen from the group consisting of in vitro testing, in vivo testing and evaluation of published lists of toxic moieties;
 - (c) selection of a cap moiety by a method chosen from the group consisting of in vitro testing, in vivo testing and evaluation of published lists of reagents with the toxic moiety;
 - (d) selection of an activation drug by a method chosen from the group consisting of in vitro testing, in vivo testing and evaluation of published lists of reagents with the cap moiety; and
 - (e) linking the differentially concentrating moiety, the toxic moiety, and the cap moiety in such a manner as to make the proto-drug itself substantially biologically inert.
4. (Original) A method of treating neoplasms in a mammal, such method comprising:
- (a) administering to a mammal in need of such treatment an effective amount of a proto-drug, such proto-drug comprising a differentially concentrating moiety, a toxic moiety and a cap moiety;
 - (b) waiting for a time delay period; and
 - (c) administering to the mammal an activating amount of an activation drug

whereby the activation drug converts the proto-drug in vivo to a pharmacologically active compound.

5. (Original) A method of converting a substantially biologically inert compound to a pharmacologically active agent, such method comprising:

- (a) administering to a mammal a proto-drug, such proto-drug comprising a differentially concentrating moiety, a toxic moiety, and a cap moiety whereby the moieties are linked together in such a fashion as to create a biologically inert compound;
- (b) waiting for a time delay period; and
- (c) administering to the mammal an activation amount of an activation drug whereby the activation drug converts the proto-drug to a pharmacologically active agent.

6. (Original) A method of selectively delivering a cytotoxic compound to tumor tissue, such method comprising administering to a mammal a proto-drug comprising a differentially concentrating moiety, a toxic moiety and a cap moiety, whereby the proto-drug delivers a cytotoxic compound to the tumor tissue in such a manner as to prevent significant damage to normal tissues by maintaining the cap moiety on the proto-drug until the proto-drug differentially concentrates in the tumor tissue during a time delay, and after such time delay the proto-drug produces a cytotoxic compound upon administration of an activation drug.

7. (Original) A pharmaceutical preparation comprising:

- (a) an effective amount of a proto-drug together with a pharmaceutically acceptable excipient; and
- (b) an activating amount of an activation drug together with a pharmaceutically acceptable excipient whereby the proto-drug and the activation drug are packaged for individual administration.

8-24. (Cancelled)

25. (Original) A method of determining a time delay period between administration of a proto-drug and an activation drug which comprises determining time T in the equation

$$R = E_A/E_B = (b_B/b_A) \exp[(b_B - b_A)T]$$

whereby:

R is the ratio of the diffusion constants of cell types A and B;

E_A is the exposure of cell type A to the proto-drug;

E_B is the exposure of cell type B to the proto-drug;

b_A is the elimination constant of cell type A; and

b_B is the elimination constant of cell type B.

26. (Original) The method of claim 25 whereby the time delay period is evaluated by in vivo procedures.

27. (Currently Amended) A proto-drug comprising:

- (a) a thioxanthone moiety that acts as a differentially concentrating moiety;
- (b) a mechlorethamine or podophyllotoxin moiety that acts as a toxic moiety; and

(c) a silane moiety that acts as a cap moiety

whereby the thioxanthone, mechlorethamine or podophyllotoxin, and silane moieties are linked to form a substantially biologically inert compound.

28-33. (Cancelled).

34. (New) An assemblage comprising a substantially biologically inert proto-drug and a substantially biologically inert activation drug, whereby the proto-drug comprises

(a) a thioxanthone moiety that acts as a differentially concentrating moiety;

(b) a mechlorethamine or podophyllotoxin moiety that acts as a toxic moiety;

(c) a silane moiety that acts as a cap moiety; and
the activation drug is a fluoride salt.

35. (New) The assemblage of claim 34 whereby the fluoride salt is sodium fluoride.